PATENT COOPERATION TREATY

# PCT



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| N.77933A JCI | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/GB00/03760 | 02/10/2000 | 01/10/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>G01N33/68 | | |
| Applicant<br>ISIS INNOVATION LIMITED et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 19/04/2001 | 11.02.2002 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br>GONCALVES M L F C<br>Telephone No. +49 89 2399 8127 |

Form PCT/IPEA/409 (cover sheet) (January 1994)

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03760

## I. Basis of th r port

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
**Description, pages:**

1-58 as originally filed

**Claims, No.:**

1-59 as originally filed

**Drawings, sheets:**

1/39-39/39 as originally filed

**Sequence listing part of the description, pages:**

1-20, filed with the letter of 20.11.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1-38 and 40-59 (part); 39.

because:

   ☒ the said international application, or the said claims Nos. 40, 41, 42 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   **see separate sheet**

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-38 and 44-59 (part); 39 are so unclear that no meaningful opinion could be formed (*specify*):
   **see separate sheet**

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | |
| | No: | Claims | 1, 12, 35 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-38, 40-59 |
| Industrial applicability (IA) | Yes: | Claims | 1-38, 43-59 |
| | No: | Claims | |

2. Citations and explanations
**see separate sheet**

While the applicant's observations have been considered, the previously expressed opinion is nervertheless maintained, at least in part, for the following reasons:

**Section III**

1. In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible (see also section V, items I.2, II.1 and III.1).

2. The application comprises claims defining the invention in terms of the result to be achieved (example claim 39) which do not comply with the requirements of Article 6 PCT. The scope of claim 39 is not defined, thus examination is not possible.

3. The application comprises claims to methods of diagnostic practised on the human or animal body, as well as claims to methods of treatment practised on the human or body (example claims 40, 41 and 42). For the assessment of such claims on the question whether they are industrially applicable, no unified criteria exists in the PCT. The patentability can also be dependent upon the formulation of the claims.

**Section IV**

1. The claims currently on file relate to three different inventions:

   I) Celiac disease diagnostic methods, agents and kits: independent claims 1, 2, 13, 14, 15, 16, 17 , 21, 22, 25, 26, 27, 28, 38, 40, 41, 42, and the claims dependent thereon;

   II) Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants: independent claims 31, 35, 46, 47, 48, 49, 51, 52, 53, 54, 55, 57, 58 and the claims dependent thereon;

III) Polynucleotides encoding mutant gliadin, cells transformed with Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin: independent claims 12, 19, 20, 29, 30, 31, 37 and the claims dependent thereon.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons: The sequence of a natural occurring homologue of gliadin or its analogue (that is the technical feature common to the abovementioned groups of claims) is already known from documents D1 to D4. The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the abovementioned groups of independent claims.

The applicant has paid the fees relative to the examination of the aforementioned three inventions.

**Section V**

**Invention I:**

Celiac disease diagnostic methods, agents and kits: independent claims 1, 2, 13, 14, 15, 16, 17 , 21, 22, 25, 26, 27, 28, 38, 40, 41, 42, and the claims dependent thereon.

I.1 The wording of claim 1 is such that the subject-matter of the claim is very broad, and consequently lacks novelty regarding the disclosures in the following documents cited in the search report (Article 33(2) PCT).

D1: O'KEEFFE J ET AL: "T cell proliferation, MHC class II restriction and cytokine products of gliadin-stimulated peripheral blood mononuclear cells (PBMC)." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104

D2: VAN DE WAL YVONNE ET AL: "Small intestinal T cells of celiac disease

patients recognize a natural pepsin fragment of gliadin." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10050-10054, XP000982626 Aug. 18, 1998 ISSN: 0027-8424

D3: TRONCONE R ET AL: "Cytokines produced by gliadin-specific T cell clones from the coeliac mucosa." GASTROENTEROLOGY, vol. 110, no. 4 SUPPL., April 1996 (1996-04), page A1031 XP000989625 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week;San Francisco, California, USA; May 19-22, 1996 ISSN: 0016-5085

D4: GODKIN A J ET AL: "Identification of a coeliac disease-specific T cell epitope from A-gliadin." GUT, vol. 44, no. SUPPL. 1, April 1999 (1999-04), page A72 XP000989626 British Society of Gastroenterology Annual Meeting;Glasgow, Scotland, UK; March 23-25, 1999 ISSN: 0017-5749

I.2 The remaining dependent and independent claims of invention I appear to relate to obvious alternatives of the method of claim 1 and are therefore not inventive (Article 33(3) PCT).

I.3 The Invention I contains a total of 19 claims, of which 17 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.

**Invention II**:

Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants: independent claims 35, 46, 47, 48, 49, 51, 52, 53, 54, 55, 57, 58 and the claims dependent thereon.

II.1 The subject-matter of claim 35, a cell **comprising** a mutant gliadin protein epitope, is anticipated by the disclosure in the following prior art document (Article 33(2) PCT):

D5: EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN (NL)) 31 March 1999 (1999-03-31) .

II.2 The remaining dependent and independent claims of invention II (Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants) appear to relate to obvious alternatives to the subject-matter of claim 35 and are therefore not based on an inventive concept (Article 33(3) PCT).

II.3 The Invention II contains a total of 14 claims, of which 13 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.

**Invention III**:

Polynucleotides encoding mutant gliadin, cells transformed with Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin: independent claims 12, 19, 20, 29, 30, 31, 37 and the claims dependent thereon.

III.1 The subject-matter of claim 12 lacks novelty regarding the disclosures in the following documents cited in the search report (Article 33(2) PCT).

D1: O'KEEFFE J ET AL: "T cell proliferation, MHC class II restriction and cytokine products of gliadin-stimulated peripheral blood mononuclear cells (PBMC)." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104

D2: VAN DE WAL YVONNE ET AL: "Small intestinal T cells of celiac disease patients recognize a natural pepsin fragment of gliadin." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10050-10054, XP000982626 Aug. 18, 1998 ISSN: 0027-8424

D3: TRONCONE R ET AL: "Cytokines produced by gliadin-specific T cell

clones from the coeliac mucosa." GASTROENTEROLOGY, vol. 110, no. 4 SUPPL., April 1996 (1996-04), page A1031 XP000989625 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week;San Francisco, California, USA; May 19-22, 1996 ISSN: 0016-5085

D4: GODKIN A J ET AL: "Identification of a coeliac disease-specific T cell epitope from A-gliadin." GUT, vol. 44, no. SUPPL. 1, April 1999 (1999-04), page A72 XP000989626 British Society of Gastroenterology Annual Meeting;Glasgow, Scotland, UK; March 23-25, 1999 ISSN: 0017-5749

D5: EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN (NL)) 31 March 1999 (1999-03-31) .

III.2 The remaining dependent and independent claims of invention III (Polynucleotides encoding mutant gliadin, cells transformed with Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin) appear to relate to obvious alternatives to the subject-matter of claim 12 and are therefore not based on an inventive concept (Article 33(3) PCT).

III.3 The Invention III contains a total of 10 claims, of which 7 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.